THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY, CHENNAI

INCIDENCE OF MALIGNANCY IN HEMITHYROIDECTOMIZED PATIENTS

DISSERTATION FOR BRANCH – I M.S., (GENERAL SURGERY)

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CERTIFICATE

This is to certify that this dissertation entitled **"INCIDENCE OF MALIGNANCY IN HEMITHYROIDECTOMIZED PATIENTS"** is bonafide work done by **Dr.D.MOHANKUMAR** under our guidance and supervision in the Department of Surgery, Madurai Medical College, Madurai submitted for the M.S., (General Surgery) BRANCH 1 EXAMINATION, to be held in March 2008, by the Tamilnadu DR.M.G.R. Medical university, Chennai.

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DECLARATION

I **Dr. D. MOHANKUMAR** solemnly declare that the dissertation titled "**INCIDENCE OF MALIGNANCY IN HEMITHYROIDECTOMIZED PATIENTS**" has been prepared by me. I also declare that this bonafide work or a part of the work was not submitted by me or any other for my award, degree, diploma to any other university & board with in India or abroad.

This is submitted to The Tamilnadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the rules & regulations for the award of M.S. (General Surgery) Branch – I to be held in March – 2008.

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INTRODUCTION

Thyroid has fascinated the surgeon for centuries; from the second millennium BC, when it has been recorded in Chinese literature. Ancient Chinese employed ground sheep's thyroid for goitre and cretinism. Thyroid malignancy has been known to exist for over three centuries. In U.K its incidence is about 0.5 % of all cancers and is responsible for fewer than 0.5 % of all deaths due to cancer. Nevertheless it has attracted the attention of surgeon, for a number of reasons.

1. Varying biological behaviour of various types thyroid malignancy

2. There is a diagnostic challenge arising out of various modes of presentation

3. Technical interest for a precise surgical approach

Even now, there is no general agreement regarding the treatment of thyroid cancer. Long history together with evolving mode of treatment has made it extremely difficult to judge the effectiveness of any single or combined therapeutic approach where in widely different view points have been expressed with great amount of convictions on either side.

AIM OF THE STUDY

These are the reasons which prompted us to undertake a study of this kind. In our institution hemithyroidectomy is being done for thyroid swellings based on preoperative clinical aid, biochemical evaluation including FNAC study.

The aim of the study is

1. To analyse the histopathological examination of hemithyroidectomy specimen for malignancy in whom the hemithyroidectomy was done for suspected benign lesions.

2. Management of those Hemithyroidectomized patients with proved malignancy, with various modalities of treatment such as completion thyroidectomy, TSH suppression with eltroxine, Radioiodine ablation, or chemotherapy.

In must be stated at the outset that in a good number of patient's prolonged follow up has not been done, as this study covers a group of patients seen in recent past nor it covers any cases treated with radioisotopes.

SURGICAL ANATOMY OF THYROID GLAND

Normal thyroid gland weighs about 20 – 25 gms. It has two lateral lobes connected by an isthmus in the midline. The lateral lobes extend along the side of the larynx from the middle of thyroid cartilage above to the sixth tracheal ring below. Lateral lobes measures approximately 5 x 3 cm (slightly larger in women). They reside in a bed between the trachea and larynx medially and two carotid sheaths and sternocleidomastoid muscles laterally.

A strong condensation of vascular connective tissue known as suspensory ligament of Berry, binds the gland firmly to each side of the cricoid cartilage and it is the ligament together with the pretracheal fascia, which splits to invest the gland, which makes the thyroid move up and down on swallowing.

Anteriorly, the thyroid lobes are in relation to the strap muscles. Situated on the posterior surface of the lateral lobes of the gland are the parathyroid glands and recurrent laryngeal nerves, which lie in

Tracheoesophageal groove just medial to lateral lobes. The pyramidal lobe of Lolouette of variable size is a long, narrow projection of thyroid tissue extending upward from the isthmus lying on the surface of the thyroid cartilage usually to the left of the prominence of that structure. It represents a vestige of embryonic thyroglossal duct and can be demonstrated in about 80% of patients at operation.

The capsule of the thyroid gland (surgical capsule) sends fibrous septa into the gland substance, dividing into numerous lobules. Each lobule consists of 30 to 40 follicles that contain colloid. These are the main secretary and storage elements.

DEVELOPMENT OF THYROID

The thyroid gland is developed from median bud of the pharynx (the thyroglossal duct) which passes from the foramen caecum at the base of the tongue to the isthmus of the thyroid.

Ultimobranchial body which arises from a diverticulum's of the fourth pharyngeal pouch of each side amalgamates with the corresponding lateral lobe. Para follicular "c" cells are derived from the neural crest and reach the thyroid via the ultimobranchial body. Recently consideration has been given to the possibility that some "c" cells are of endodermal rather than neural crest origin.

BLOOD SUPPLY

The arterial supply is rich and extensive anastomosis occur between the main thyroid arteries and branches of tracheal and oesophageal arteries. The main supply is via two paired arteries. A third vessel occasionally supplies the lower pole of one or other side.

The superior thyroid artery, the first branch from the anterior aspect of external carotid, after giving off its sternocleidomastoid and superior laryngeal branches pierces the pre-tracheal fascia as a single vessel to reach the summit of the upper lobe. The external laryngeal nerve is immediately behind the artery as the vessel approaches the upper pole. In

thyroidectomies, the artery is ligated right at the pole, to avoid damage to the nerve.

The artery divides on the gland into an anterior branch that runs down to the isthmus and a posterior branch that runs down to the back of the lobe and anastamoses with anterior ascending branch of the inferior thyroid artery from the lower pole. A separate branch from the left artery may supply the pyramidal lobe.

The inferior thyroid artery is generally much larger than the superior thyroid artery but it is less constant, being absent or duplicated on one side or other in 10% of individuals. It arises from the thyrocervical trunk and passes upward for a variable distance before looping down running medially behind the carotid sheath to reach the posterolateral aspect of the gland at the junction of middle and lower thirds.

The suspensory ligament always contains small branches. The recurrent laryngeal nerve has a variable relationship to the artery but always lies behind the pretracheal fascia. If this structure remains intact

during thyroidectomy, the nerve will not have been divided. It is close behind the fascia. However may be bruised or caught in a ligature; hence the preference of some but not all surgeons ligating the inferior thyroid artery well lateral to the gland before it begins to divide into its terminal branches.

Numerous unnamed accessory arteries arise from the oesophagus and trachea, but the most frequently encountered is the thyroidea ima (Neubauers' Artery) which enters the lower part of the isthmus in 3% of individuals. It springs from the brachiocephalic trunk, right common carotid artery or direct from the arch of aorta and represents a persistent embryonic vessel that usually disappears. In the absence of inferior thyroid artery on one side, Thyroidea ima artery may be the principal source of blood supply to the lobe and therefore substantial.

Venous plexus forms under the capsule. The named thyroid veins although three in number like the arteries are subject to greater variation.

The superior thyroid vein, formed by a confluence of vessels from the upper pole crosses the common carotid artery high in the neck to drain into the internal jugular vein, which overlies the inferior thyroid artery, also ends in the internal jugular vein after crossing the common carotid artery.

The internal jugular or brachiocephalic vein in the anterior mediastinum and are intimately associated with the thyrothymic ligaments, which expand inferiorly as the lobes of thymus.

INNERVATION

The bulk of sympathetic (vasoconstrictors) supply is derived from the middle cervical ganglion and enters the gland on the inferior thyroid artery. Some fibres from the superior cervical ganglion travel with the superior thyroid artery. The parasympathetic fibres are derived from the vagus and reach the gland via branches of laryngeal nerves.

LYMPHATIC DRAINAGE

The thyroid is generously supplied with lymphatics and a rich network ramifies throughout the gland. They drain primarily into the mediastinal nodes inferiorly, tracheo- oesophageal nodes laterally and the midline delphian nodes superiorly.

From the lower pole they pass with the inferior thyroid artery back to its origin from the subclavian behind the carotid sheath into the postero inferior group.

IMPORTANT ANATOMICAL RELATIONSHIPS

Vagus nerve having entered the mediastinum gives off the recurrent nerves, which return to the neck having circled around the arch of aorta on the left and the right subclavian artery on the right.

It ascends in the tracheo-esophageal groove and has variable relationship with the inferior thyroid artery on each side. Occasionally, the nerve divides itself early and branches around the artery in 10% of

individuals. In approximately, 0.25% of individuals the recurrent laryngeal nerve on the right is non-recurrent but passed directly from the vagus to cricothyroid muscles.

As it takes the same course as the inferior thyroid artery, it is particularly vulnerable if its presence is unrecognised when this vessel is routinely ligated laterally. The recurrent laryngeal nerve innervates the intrinsic muscles of the larynyx except for the cricothyroid muscle. Damage to this nerve leads to vocal cord paralysis on the same side.

Riddell indicated that among cases in which surgeons"avoid "rather than expose the recurrent laryngeal nerve there is incidence of vocal cord damage. It is very important for the surgeon to carefully identify this nerve at the time of operation.

SUPERIOR LARYNGEAL NERVE

This also arises from the vagus (inferior ganglion) and divides at the level of hyoid bone into a large internal laryngeal nerve and a small external laryngeal nerve. The latter runs close to the superior thyroid

artery but at a deeper plane. Immediately above the superior pole of thyroid, it terminates as the nerve supply to the cricothyroid muscle which acts as tensor of vocal cords on the same side.

THE CERVICAL SYMPATHETIC CHAIN

This underlies the carotid sheath just medial to the vagus on the pre-tracheal fascia and is in close proximity to the inferior thyroid artery as it arches around medially.

PARATHYROID GLANDS

There are normally four parathyroid glands, the upper pair of which lies in close proximity to the dorsal aspect of thyroid. They are usually found above and medial to where recurrent laryngeal nerve crosses the inferior thyroid artery, frequently tacked round behind its branches. The lower parathyroid gland on each side is situated within a 2 cm radius of the lower pole of thyroid typically on its surface anterolaterally and at a level below and medial to where the recurrent laryngeal nerve crosses the inferior thyroid artery.

PHYSIOLOGY

The thyroid, largest endocrine gland in the body produces three hormones. Thyroxine (T4), tri-iodo thyronine (T3) and calcitonin. T4&T3 are both stored in the colloid consisting primarily of thyroglobulin which is an iodinated glycoprotein. Thyroglobulin stores are dependent on adequate dietary iodine intake, which is essential for T3 & T4 synthesis.

Iodine is derived mainly from milk and diary products with a smaller proportion from salt, water and fish and iodised salt. Plasma levels of iodine vary widely, depending on geographical locality. Iodides are absorbed in the stomach and the upper gastrointestinal tract approximately two-thirds is excreted via kidneys and one-third is trapped in the thyroid where 90% of body stores of iodine are found.

The steps in the synthesis of thyroid hormone are:

1. Concentration of iodine in the gland.

2. Rapid oxidation of iodides to iodine by a peroxidase enzyme system.

3. The formation of precursor amino acids: 3-mono-iodothyronine (MIT) and 3-5 Di-iodothyronine (DIT) and

4. The coupling of these inactive iodothyronines to form the hormonally active iodothyronines & Tri-iodothyronine and Thyroxine (T4). When iodine transport is defective, because of either pharmacologic inhibitors or spontaneous disease, goiter and or hypothyroidism result.

The hormonally active T4 & T3 & iodothyronines are held in peptide linkage with a specific protein, thyroglobulin which forms the major component of intra follicular colloid.

Release of active hormone into circulation involves hydrolysis of the throglobulin by proteases and peptidases resulting in T4 & T3. The activity of these enzymes is enhanced by administration of TSH.

Thyroid stimulating hormone produced by thyrotrophic cells of anterior pituitary control the complex enzymatic reactions that trap iodine, convert it into T4 & T3 and release it into the circulation. When T3 & T4 raises above the normal range, TSH production is shut down by a negative bio-feed back loop.

Release of TSH is regulated by Thyrotrophin releasing Hormone (TRH) which is produced in the hypothalamus. TRH enters the capillary bed of the stalk median eminence, passing via portal veins and sinusoids to bathe the anterior pituitary cells. TSH biosynthesis shows a circadian rhythm, its secretion will be maximum in the evening before the onset of sleep, remaining high overnight and falling to a low around mid-day.

The role of calcitonin in normal physiology has not been established in men, but it may be involved in the regulation of plasma calcium and phosphate metabolism. However, thyroidectomy which removes all Para follicular “c” cells causes no disturbances of calcium homeostasis.

The rise in plasma calcitonin which occurs during pregnancy and lactation appears to have no effect on maternal skeleton but calcium resorption may be prevented by a concomitant increase in the level of circulating cholecalciferol.

SURGICAL PATHOLOGY

CLASSIFICATION OF THYROID MALIGNANCY

PRIMARY

Follicular epithelium – differentiated

- Follicular 17%
- Papillary 60%

Follicular epithelium undifferentiated

- Anaplastic 13%

Lymphoid cells

- Lymphoma 4%

Para follicular

- Medullary 6%

SECONDARY

- Metastatic
- Local infiltration

DEGROOT'S CLINICOPATHOLOGICAL STAGING:

Stage 1 - Tumors with single or multiple intrathyroidal foci.

Stage ll - Tumors with cervical metastases that are not fixed and are without invasion.

Stage lll - Tumors with fixed cervical metastases or tumors with local cervical invasion beyond the thyroid capsule.

Stage lV - Metastases outside the neck.

TNM staging of thyroid malignancy (AJCC 2002)

T_0 - No evidence of Primary tumor

T_1 - Tumor 2 cm or less in greatest dimension limited to thyroid

T_2 - Tumor >2cm but not more than 4 cm in greatest dimension limited to thyroid

T_3 - Tumor > 4 cm limited to thyroid or with minimal extra thyroidal extension

T_{4a} - Any tumor extending beyond thyroid capsule to invade subcutaneous soft tissues, larynx, trachea, oesophagus, RLN

T_{4b} - Tumor invades prevertebral fascia or encases carotid artery or mediastinal vessels

N_0 - No palpable lymph nodes

N_1 - Regional nodal metastases

N_1a - Level VI (Pretracheal, paratracheal & prelaryngeal / Delphian nodes

N_1b - Unilateral, bilateral or Contralateral cervical or mediastinal nodes

M_0 - No distant metastases

M_1 - Distant metastases

Differentiated thyroid cancer risk group definitions (From Lahey Clinic Foundation)

Low Risk Group

A		All younger patients without distant metastases (men < 41 ; women < 51 years)
B		All older patients with :
	1.	Intra thyroidal papillary cancer or follicular cancer with minor capsular involvement
	2.	Primary cancers < 5 cm in diameter
	3.	No distant metastases

High Risk Group

A		All patients with distant metastases
B		All older patients with :
	1.	Extra thyroidal papillary cancer or follicular cancer with major tumor capsular involvement and
	2.	Primary cancers < 5 cm in diameter or larger regardless of extent of disease

PAPILLARY CARCINOMA

This is the most common type of thyroid cancer, which runs a slow clinical course. Peak incidence occurs in 3rd to 4th decade. Female to male ratio is 3:1. Most commonly presents as thyroid swelling.

Histological subtyping by Hawk and Hazard

1. Pure papillary
2. Mixed papillary and follicular
3. Follicular variant of papillary
4. Tall cell variant

The cancers are often multicentric within thyroid gland. 33 to 40% cases exhibit microscopic or gross tumor involvement within contra lateral lobe.

Macroscopically tumor is grayish white, poorly defined nodule of varying size with areas of hemorrhagic necrosis, cyst formation with occasionally visible papillae.

Microscopically there appears neoplastic epithelium on fibro vascular stalks often projecting into cystic spaces. Epithelium is usually single layer and cubical with homogenous cytoplasm, surrounding ovoid nucleus with fine chromatin and optically clear appearance often called “ORPHAN ANNIE NUCLEI”. Laminated calcified spherules called “PSAMMOMA BODIES” are present in 40%.

10 year survival rate is 84%. However with extra thyroidal spread it falls to 50%.

MINIMAL PAPILLARY CARCINOMA

Lesions less than 1cm without local invasion or lymph node metastasis, often found as an incidental finding in thyroidectomy specimen operated for another benign lesion

OCCULTPAPILLARY CARCINOMA

Primary lesion less then 1.5cm which are often impalpable.

FOLLICULAR CARCINOMA

Incidence is 10 to 18%. It tends to occur in old age with peak incidence in fifth decade. They often present as single, solid expansile tumor mostly unencapsulated. Multifocality and lymphatic spread is uncommon. Metastasis by blood stream is common.

Macroscopically they appear unencapsulated and invasive nature is apparent only histologically. Microscopically various sized follicles and trabecular cords of cuboidal neoplastic cells with compact hyperchromatic nuclei and mitosis. Capsular and vascular invasion are prominent features.

The tumor and its metastases are most part functional in that they take up radioiodine, which gives an important therapeutic option. Prognosis depends on the extent of invasion and distant metastases. In their absence, 10-year survival rate is 72% but in their presence, it is only 44%.

HURTHLE CELL TUMOUR

This is considered as a variant of follicular neoplasm. Microscopically the cells are arranged in sheets with eosinophilic cytoplasm (Askanazy cells). In electron microscopy, cytoplasm is packed with mitochondria.

Incidence of carcinoma in Hurthle cell tumor varies between 5.32 to 62% in different clinical series. Histologically benign lesions however latter metastasized in 2.5 to 11.5% of patients. The cells are less likely to concentrate radio iodine.

MEDULLARY CARCINOMA

It is a C-cell calcitonin producing tumor of thyroid. 80% case are sporadic and 20% are associated with multiple endocrine neoplasia II, which occurs in family with autosomal dominant trait. Familial cases are often multifocal and bilateral.

Calcitonin secreted by the tumor cells is used as a tumor marker. Carcinoembryonic antigen is also elevated in most of the patients.

Patients are usually presented with thyroid nodule associated with cervical lymphadenopathy in 20% and symptoms like dysphagia, diarrhea may be a prominent feature and episodic flushing may also occur which are all due to serotonin, prostaglandin E2, F2 alpha secreted by the tumor. The tumor shows no sex predilection.

Macroscopically tumor appears as firm grayish, finely calcified mass. Microscopically nests of closely packed polygonal cell with eosinophilic granular cytoplasm and hyper chromatic nuclei, set in fibrous stroma that stains for amyloid and may show calcium deposits.

The tumor tends to have protracted course. Dissemination occurs by lymphatics as well as by blood stream. Overall 10 year survival rate is 57%.

ANAPLASTIC CARCINOMA

It commonly occurs in 7^{th} to 8^{th} decade. Its incidence is higher in endemic goitre area. It has been proved that many of these tumors arise from pre existing differentiated thyroid malignancy as a result of the original tumor is undiagnosed or inadequately treated. Clinically it

presents with rapidly enlarging thyroid swelling usually with respiratory distress.

Macroscopically tumor is firm and white with areas of necrosis, replacing thyroid and extending into adjacent structures.

Microscopically three types are recognized.

1. Spindle cell variant with cells in bundles or whorls resembling sarcoma with numerous mitoses.

2. Small cell variant consisting of round cells with hyper chromatic nuclei and scanty cytoplasm.

3. Giant cell variant with spindle cells and bizarre pleomorphic giant cells with frequent atypical mitoses.

   Prognosis is poor. Over all 5 year survival is 10 – 15%. 75% patients die with 1 year.

LYMPHOMA

It occurs frequently in middle to old aged women, presenting with rapidly enlarging painless mass in thyroid. It is due to NHL in all patients.

Coexistent Hashimoto's thyroidits occurs in most patients. It has been suggested that chronic antigenic stimulation of lymphocytes causes transformation into lymphoma cells.

Over all 5 year survival is 86% if the lesion is confined to thyroid but falls to 38% with extra thyroidal diseases.

METASTATIC CARCINOMA

It is present in 2 – 4 % of patients dying of malignant disease. Bronchogenic carcinoma accounts for 20% thyroid secondary deposits. At autopsy 3% of all Bronchogenic carcinoma demonstrates thyroid metastasis. The other common tumours metastasizing to thyroid are from breast, lung, kidney or malignant melanoma.

Clinically they may appear similar to primary thyroid cancer but microscopically they differ. Direct extension from adjacent carcinoma may involve thyroid. This type of malignancy is associated with poor prognosis.

NATURAL HISTORY AND PATHOGENESIS

Development of thyroid tumor is intimately associated with

1. Iodine deficiency

2. TSH stimulation

The process of oncogenesis conceived to be a series of events introduced by genetic and environmental factors which alter growth control.

Van middlesworth (1988) pointed out that iodine deficiency may increase the invasiveness of thyroid cancer through TSH stimulation.

As pointed out by **Sarda A.K et al., (Brit. J. Surg. Nov. 1986)**. The TSH levels in patients presenting with solitary nodular thyroid carcinoma was significantly higher than the benign solitary nodule. The mean TSH level of non – solitary thyroid nodular carcinoma was in high normal range.

Also shown by **Bubenhofer and Holdinger (Br. J. Surg. Nov.1986)** that on reexamining all their patients with thyroid cancer from

Zurich (1924 – 1974), they found a relative reduction of anaplastic cancer after iodine prophylaxis.

Some of the following factors can affect the natural progress of disease.

1. ROLE OF RADIATION

It is now generally recognized that external beam radiotherapy to treat benign and malignant conditions of head and neck can bring both benign and malignant nodular changes in thyroid. It has been demonstrated that there is a straight line increase in incidence up to a dose of about 1500 rads, but only after a mean latency of 25 years or more. **Refetoff et al . ,** found that 25% had palpable abnormally of thyroid and 6.8% of total group have thyroid cancer.

Papillary carcinoma is the usual type associated with radiation exposure. It is now shown that high dose radiation (i.e) > 2000 rads also increases the prevalence of thyroid cancer, which was once thought to be of no risk to thyroid.

The risk of exposure from radioisotope study of thyroid has also been implicated. Now in many hospitals 1^{123} or 99m Tc instead of 1^{131} is being used as a preventive action, since thyroid exposure is greatly diminished.

2. GOITRE

In a good number of patients with carcinoma of thyroid there is a preexisting goitre was present for a long time. In **Fosters** series incidence of malignancy in patients operated for non toxic goitre was about 10%.

A good number of patients operated for non toxic single nodular goitre have turned to be malignant. The proportion of such adenomas turning malignant had been 15.8% in **Ward** series, 24.5 % in **Crile** series, 24.4% in **Cole** series, and 25% in **Shaw** series (Tata Memorial). In **Our study**, this is about 16.7%.

The association of papillary carcinoma with Hashimoto's thyroiditis was observed in Mayoclinic and it appears to be protective against development of postoperative tumor recurrence.

3. HORMONAL FACTORS

The striking preponderance of thyroid cancer in females raises the possibility of female sex hormones as an etiological factor. In one study, an independent and increasing risk was observed with increasing total number of pregnancy. In another series women who had a history of breast cancer were almost three times more likely to develop thyroid cancer. More recent study show that late menarche and late age at first pregnancy predisposing to increased risk for developing thyroid cancer. However, the mechanism remains obscure.

MATERIALS AND METHOD

Our study covers the result of analysis of 72 patients who underwent hemithyroidectomy based on preoperative investigations which suggested benign lesions, but the histopathological examination proved to be malignant. The period of study was 2½ years from May 2005 to October 2007 in our institution. The criteria for patient selection were

1. Clinically solitary nodule of thyroid
2. No suspicious lymphnode enlargement
3. Clinically Euthyroid
4. Clinically no adjacent structure invasion or any distant metastasis
5. FNAC of thyroid showed follicular neoplasm or benign lesions
6. Otherwise, general condition is fit for surgery

All the 72 patients underwent Hemithyroidectomy and biopsy reports were taken for our study, and the patients were subsequently followed up.

CLINICAL STUDY

AGE AND SEX INCIDENCE

In our study, the minimum age was 19 years and the maximum was 60 years. Male to female ratio was 1:8.9.

Age group In years	Female	Male	Total
< 20	7	1	8
21 – 30	16	1	17
31 – 40	20	0	20
41 – 50	15	4	19
>51	7	1	8
Total	65	7	72

INVESTIGATIONS

Apart from routine blood investigations, the following specific investigations were done.

1. Ultra sonogram of the thyroid gland.
2. Thyroid hormonal profile including total T4, T3 and TSH level.
3. Fine needle aspiration cytology of the thyroid swelling.

FNAC study of the thyroid swelling was done and the interpretations were as follows.

	Number	**Percentage (%)**
Follicular neoplasm	20	27.8
Non Neoplastic Goitre	52	72.2

All the 72 patients underwent hemithyroidectomy, our pathologist did histopathological examination of the specimen, and the interpretations were as follows:

	Number	**Percentage (%)**
Follicular Adenoma	48	66.7
Papillary Carcinoma	9	12.5
Follicular Carcinoma	3	4.2
Adenomatous Goiter	4	5.5
Hashimoto's Thyroiditis	4	5.5
Lymphocytic Thyroiditis	1	1.4
Follicular Adenoma with Papillary Hyperplasia	1	1.4
Follicular Adenoma with Lymphocytic Thyroiditis	1	1.4
Total	**72**	**100.0**

The number of patients who presented with malignancy in their hemithyroidectomy specimen was 12. The incidence was 16.7%

	Number	Percentage (%)
Papillary Carcinoma	9	12.5
Follicular Carcinoma	3	4.2
Total	12	16.7

The ratio of papillary to follicular carcinoma in our study was 3:1.

Sex related incidence of malignancy in hemithyroidectomized patients as follows:

	Male	Female
Papillary Carcinoma	1	8
Follicular Carcinoma	0	3

Age related incidence as follows:

Age Group	Number
<20	1
21 - 30	5
31 – 40	4
41 – 50	0
>50	2

The malignancy is common in third and fourth decades in our study.

MANAGEMENT

After diagnosing malignancy in hemithyroidectomized patients, further treatment was planned based on risk factors as well as patients willingness.

Our patients were managed by

1. Completion Thyroidectomy followed by suppressive dose of thyroxin

2. Suppressive dose of thyroxine alone for TSH suppression

1. COMPLETION THYROIDECTOMY FOLLOWED BY SUPPRESSIVE DOSE OF THYROXINE

This was done in four patients

1. One male patient with papillary carcinoma

2. Two female patient with papillary carcinoma

3. One female patient with follicular carcinoma

METHOD OF COMPLETION THYROIDECTOMY

By excising the old scar skin flaps were raised. Strap muscles which were adherent with thyroid capsule, carefully released and after ligating vascular pedicle, completion thyroidectomy was done. Every effort was made to safeguard both parathyroids as well as recurrent laryngeal nerve. The wound was closed with vacuum drainage.

II. SUPPRESSIVE DOSE OF THYROXINE ALONE FOR TSH SUPPRESSION

It was offered to remaining 8 patients who were not willing for re-operation the dose was 0.3mg per day and the patients were subjected regular follow up after explaining the risk of malignancy.

III. RADIO IODINE THERAPY

It was not given to any patients because of non availability.

IV. EXTERNAL RADIOTHERAPY & CHEMOTHERAPY

No external radio therapy and chemotherapy was given.

The completion thyroidectomy specimens were subjected to histopathological examination and the results were as follows.

Papillary Carcinoma	1
Follicular Carcinoma	0
No evident of Malignancy	2
Well encapsulated follicular adenoma	1

POST OPERATIVE FOLLOW-UP

After surgery, the patients resumed normal diet on the next day of surgery. Antibiotics were exhibited for 5 – 7 days. Drains removed after 24 – 48 hours. Sutures were removed on 6 – 7 days. Patients were back to home on 8^{th} day with advise to attend regular follow up. No morbidity was reported after hemithyroidectomy.

After completion thyroidectomy, out of four patients, we had transient hypocalcaemia in one patient and another patient with transient

vocal cord plasy. Later both patients recovered completely with conservative treatment. No permanent hypocalcaemia or permanent vocal cord plasy was noticed in our patients. After completion thyroidectomy the patients were put on suppressive dose of thyroxin 0.3mg per day and advised for regular follow-up.

PROGNOSIS AND FOLLOW-UP

The average period of follow-up in our study was 4 – 24 months. During follow-up, through clinical examination was done to detect the recurrence or metastasis in the cervical nodes. So far no one of our patients developed any complication like local recurrence or nodal metastasis.

The dose of thyroxin therapy was adjusted to keep the serum TSH level undetectable or less than 0.1 to 0.3 mU/L. none of them have so far developed any toxic symptoms. All the patients were doing well so far. Follow-up with 1^{131} scan or with serial estimation of thyroglobulin assay was not done because of the non-availability.

DISCUSSION

We reviewed the world literature and references for our study. The incidence of malignancy in hemithyroidectomized patients as revealed in world literature is as follows.

Authors	Incidence In %
Fredrich et al.,	24.3
Adwok et al.,	15.0
Crile et al.,	24.5
Ward et al.,	15.8
Cole et al.,	24.4
Gharib et al.,	25.0
Aschraft et al.,	16.0
DH Shaw (Tata Memorial)	25.0
Our study	16.7

Incidence of malignancy in solitary nodule of thyroid for which the hemithyroidectomy was done ranges from 11 – 20% **(Kendall & Condon 1969, Pasarras et al, 1972)**. The reported incidence where solitary nodule goitre turning into malignancy was already discussed.

In a study by **C.F.J. RUSSEL (UK)** who performed hemithyroidectomy for solitary nodule of thyroid, the incidence of malignancy among those 61 patients was about 13%.

In the world literature, accuracy of FNAC is 70 – 97%. Although FNAC provides useful information regarding nature of thyroid swelling the reported incidence of false negative reports is significant and is about 17% **(CUSI K. et al., 1990)**. Therefore, it is clear that a negative report for malignancy from FNAC study should be cautiously interpretated. If thyroid cancers are not be missed a liberal policy of surgical resection of thyroid should be done preferably a hemithyroidectomy. More over FNAC cannot differentiate follicular adenoma from follicular carcinoma.

Some authors' experience with FNAC and final pathological diagnosis is discussed below.

Authors	FNAC (Benign and Indeterminate)	Histopathologically malignant	Percentage (%)
Altavilla et al., 1990	213	26	12.2
Hamming et al., 1990	133	9	6.8
Caplan et al., 1991	127	34	26.8
Layfield et al., 1991	90	22	24.4
La. Rosa et al., 1991	622	68	10.9
Klemi et al., 1991	174	10	5.7
Wax M.K. et al., 1992	244	32	13.0
Piromalli et al., 1992	138	23	16.7
Our study 2007	72	12	16.7

It has been recommended that incidental papillary cancer detected following surgery for benign thyroid disease confined within the capsule of the thyroid are indolent tumors with little if any clinical significance. The completion thyroidectomy is not advised for all cases they may be put on suppressive dose of thyroxine and closely observed **(Surgical Clinical of North America, June 1995).**

But it has been proved that the residual malignant focus is found in contra lateral lobe in 50% patients with papillary carcinoma and in 33% with follicular carcinoma. Incidence of recurrence in opposite lobe is 7 – 10%, so completion total thyroidectomy is justified in patients who have thyroid carcinoma 1cm or greater. **(Endocrinology and metabolism clinics of North America, march 1996).**

Completion thyroidectomy was done in four of our patients, in whom three patients with papillary carcinoma and one patient with follicular carcinoma because the size of the tumor was 4cm and above preoperatively.

Further more completion thyroidectomy facilitates 1^{131} scan to be done at later time for detections of metastasis because presence of normal thyroid tissue competes with metastases for radio iodine obtained.

We referred the world literature for completion thyroidectomy. An analysis of the derived references was discussed below:

	Wax M.K. et al., University of virginia (1992)	**Miccoli P. et al., Italy (1998)**	**S.K.Mishra et al., SGPGIMS, Lucknow 1989 - 97**	**Our study 2005 - 2007**
No. of completion thyroidectomy	32	19.0	22.0	4
Residual Foci (%)	2	15.8	55.0	25
Transient Hypocalcaemia (%)	15	0	18.2	25
Transient RLN Palsy (%)	3	0	9.1	25
Permanent Hypoparathyroidism (%)	3	0	0	0
Permanent RLN Palsy (%)	0	0	0	0
Mortality (%)	0	0	0	0

It is evident from the above studies that completion thyroidectomy can be done safely with minimal morbidity and no mortality **Rao et al and Levin et al** showed that in their study completion thyriodectomy are safe with low mortality.

RADIOIODINE ABLATION

None of our patients were treated with radio iodine. The dose of 1^{131} required for ablation of contra lateral lobe is high which carries risk of leukaemia and lymphoma (De Groot L.J et al). Bandeson et at, reported a series of 10 parathyroid adenoma that developed in patients who received 1^{131} ablation .Because of these reasons 1^{131} ablation is not much useful in treating remaining thyroid tissue.

It has been recommended and proved that in low risk patients the type of surgery does not affect the survival adversely.

Wolff H.et al (1979-1988) reported 5 years survival rate for differentiated thyroid cancer was from 81.5% to 100% in stage T1N0M0 (microcarcinoma) for the patients who underwent less radical procedures like hemithroidectomy (Zentral bl-Chir 1989;114(18):1202-8).

In another study at university of Rome by Russo et al(1997). Among 16 patients with microcarcinoma, 8 underwent total thyroidectomy and another 8 underwent hemithyroidectomy, and observed that there was no difference in long term results between different surgical treatment for microcarcinoma of thyroid. (**Minerva Chir, 1997 July-August 52(7-8) 891-900**).

Brooks et al., treated 222 patients with differentiated thyroid carcinoma with total thyroidectomy (43 patients) or less than total thyroidectomy (179 patients) and found no differences in recurrence or survival rate. They believe that patients with occult papillary thyroid carcinoma or follicular carcinoma with minimal capsular invasion can be treated with thyroid lobectomy and isthumectomy, because the prognosis after such treatment approaches 100%.

Woolner et al agree that treatment of choice for occult papillary carcinoma is Hemithyroidectomy and isthumectomy followed by TSH suppression. Because, inspite of multicentricity is high, there is extremely low incidence of clinical carcinoma in opposite lobe after hemithyroidectomy and TSH suppression.

CONCLUSION

Based on our study certain conclusion is arriving at incidence of malignancy in Hemithyroidectomized patients are 16.7% which correlates with world literature (15%-25%).

FNAC results showing benign lesions should be cautiously interpreted because of significant false negative reports. Conclusive reports can not be obtained by FNAC in follicular carcinoma.

Most of the incidentally discovered malignancies following Hemithyroidectomies are papillary type (papillary to follicular ratio is 3:1)

Most of these tumours can be regarded as occult and minimal because they rarely show evidence of extrathyroidal spread in papillary carcinoma or major capsular invasion in follicular carcinoma. These tumours mostly follow a benign course even with the risk of recurrence in

the contralateral lobe. Completion thyroidectomy offers effective treatment in a group of selected patient's with minimal morbidity.

In low risk patients supplementary dose of thyroxin for TSH suppression offers equally efficient therapeutic option.

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PROFORMA

INCIDENCE OF MALIGNANCY IN HEMITHYROIDECTOMIZED PATIENTS

Name	:	Case No	:
Area of Residence	:	I.P.No.	:
	:	Age/Sex	:
		Ward	:
Occupation	:		

CLINICAL PRESENTATION

Duration	:	Past History	:
Side	:	Personal History	:
Pain	:	H/o irradiation	:
Dysphagia	:	Toxic Symptoms	:
Voice Change	:		
Family History	:		

CLINICAL EXAMINATION

Side	:	Pressure Signs	:
Size	:	Nodal Status	:
Position	:	Spine and Cranium	:
Consistency	:	Cardiovascular System:	
Fixity	:	Respiratory System	:
Carotids	:	Abdomen	:
Eyes	:	Others	:
FNAC	:		
Diagnosis	:		

INVESTIGATIONS

HB%	:	X-ray neck	:
TC	:	X-ray chest	:
DC	:	ECG	:
ESR	:	BP	:
Urine : ALB	:	USG NECK	:
: SUG		ENT opinion	:
Blood Urea	:	Blood Group	:
Blood Sugar	:	Rh Typing	:

T3	:	FNAC	:
T4	:	TSH	:
Others	:		

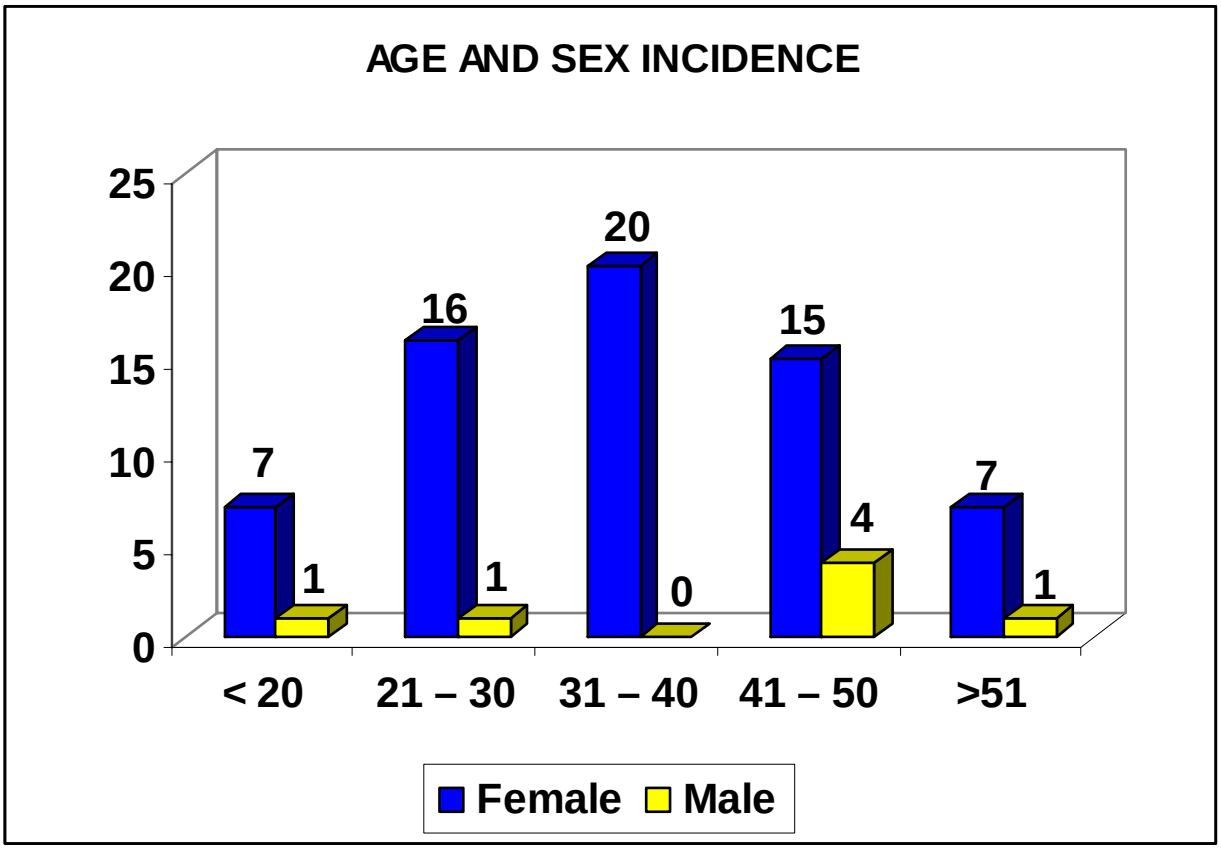
Medical endocrinology opinion

MANAGEMENT

Hemithyroidectomy	:	Biopsy	:
Completion			
Thyroidectomy	:	Biopsy	:
Thyroxin Alone	:		
Complications	:		

FOLLOW UP

Hormonal Therapy	:
Radio Iodine	:
Chemotherapy	:
Radiotherapy	: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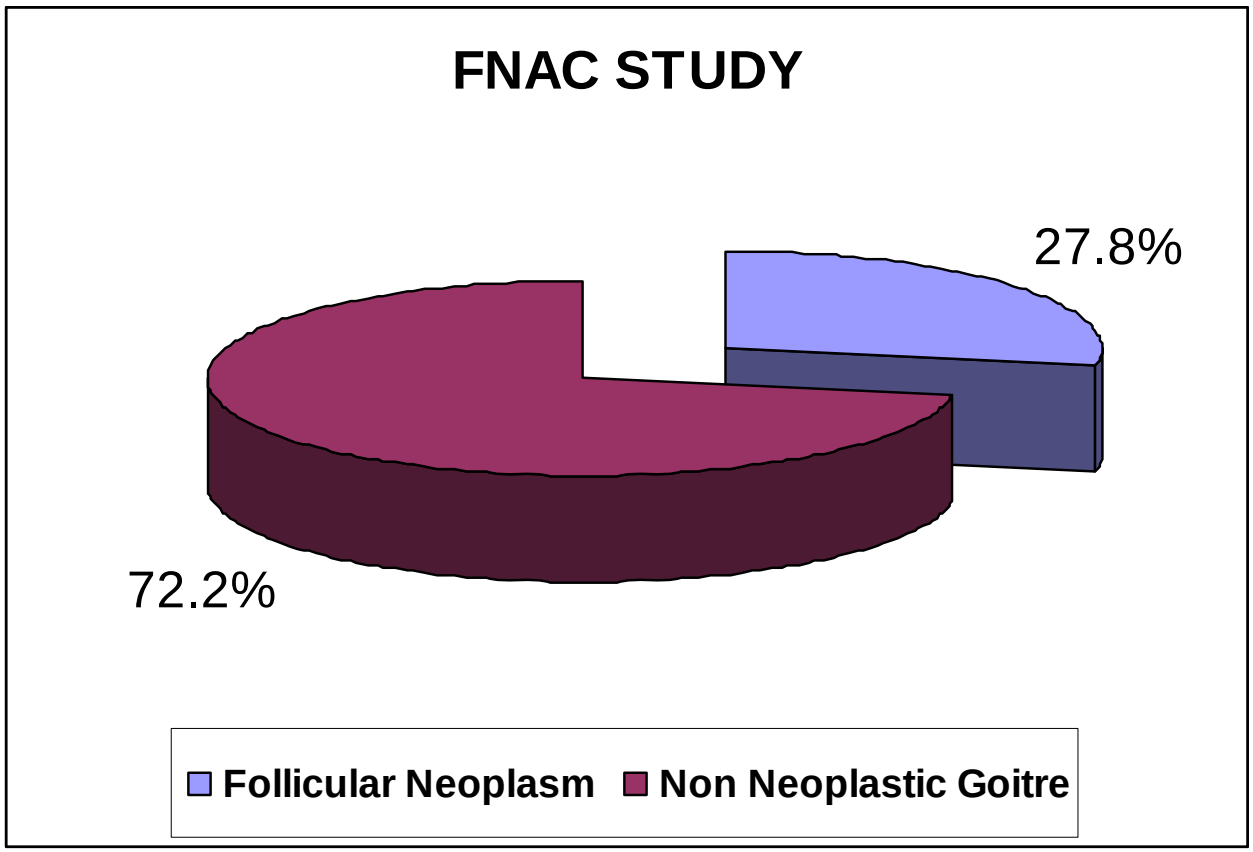
21 – 30
31 – 40
41 – 50
>51
Female
Male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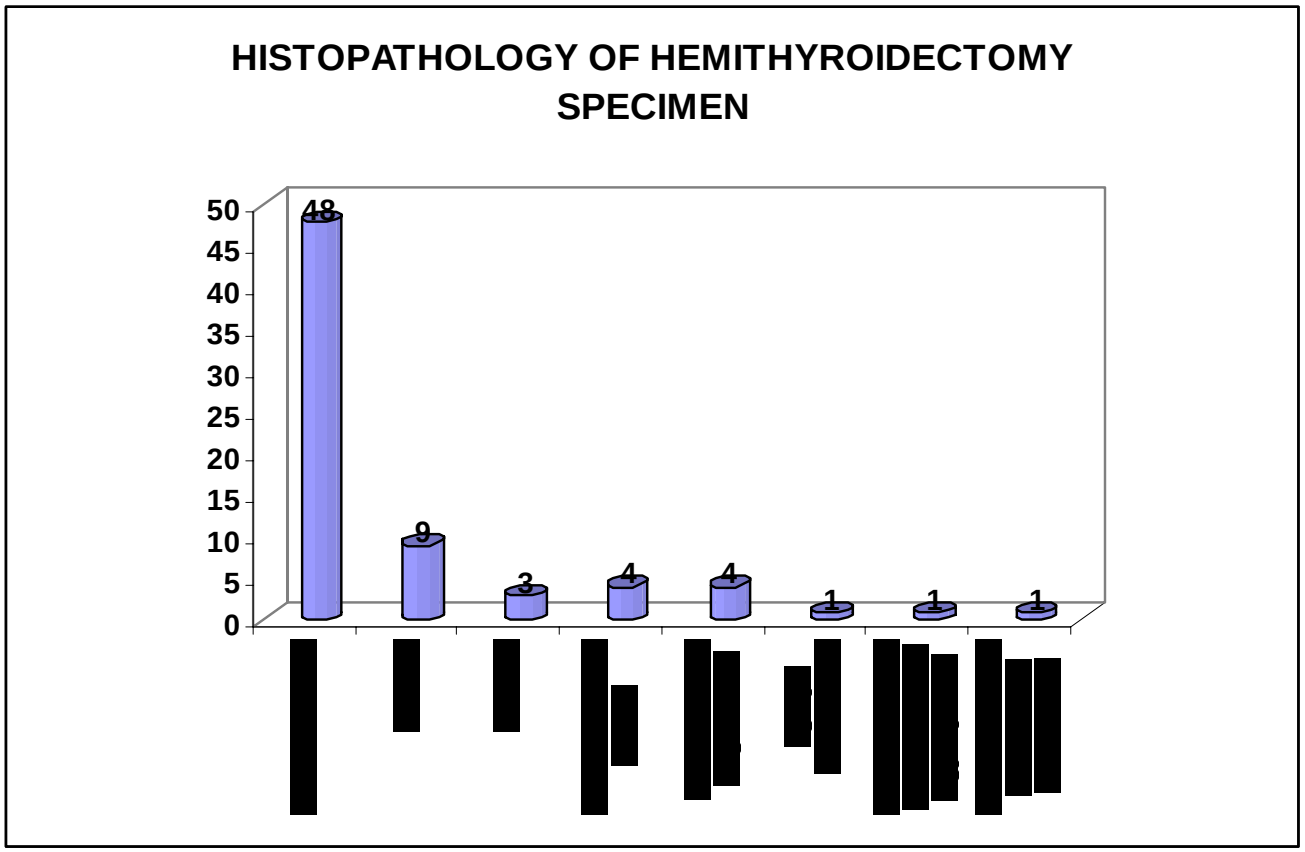
72.2%
Follicular Neoplasm
Non Neoplastic Goitre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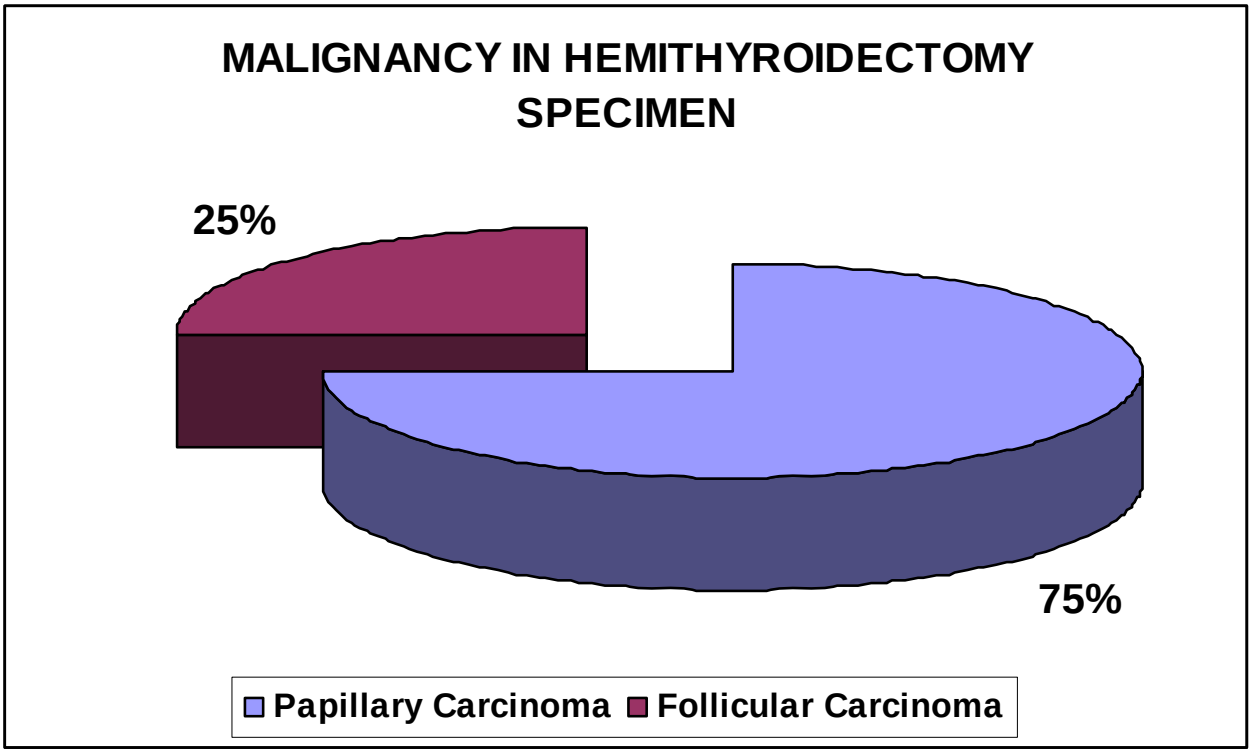
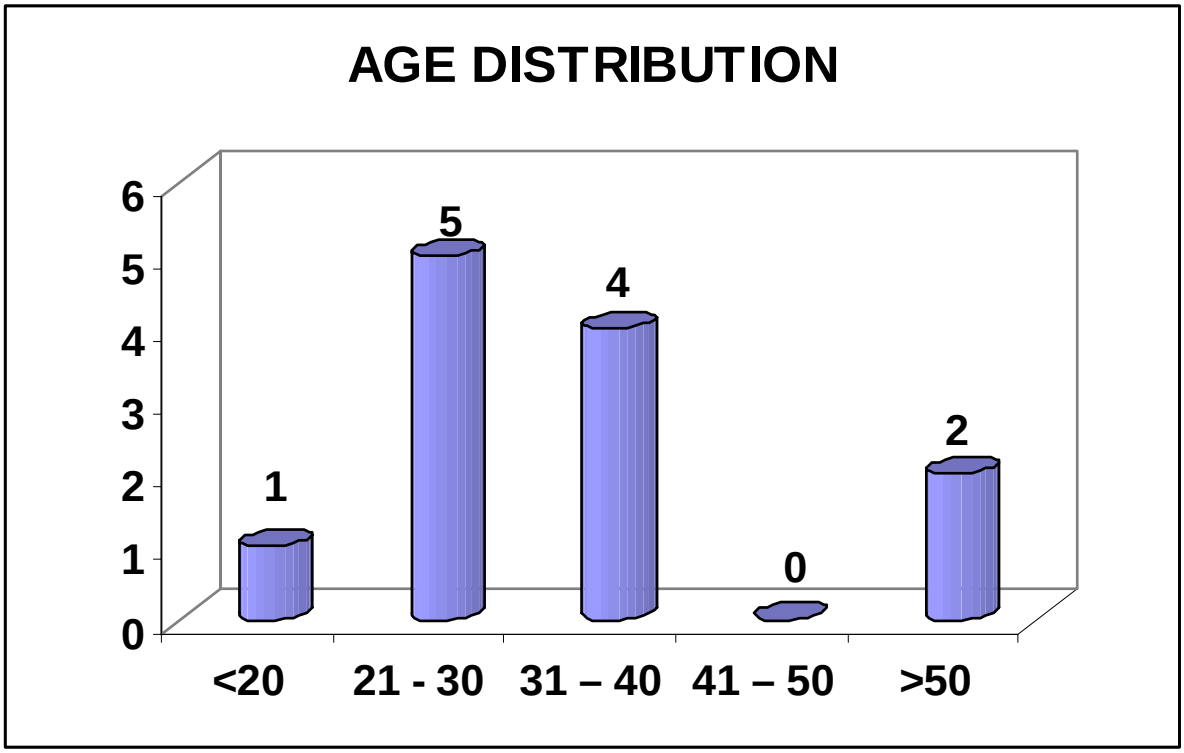

MALIGNANCY IN HEMITHYROIDECTOMY SPECIMEN
25%
75%
Papillary Carcinoma
Follicular Carcinoma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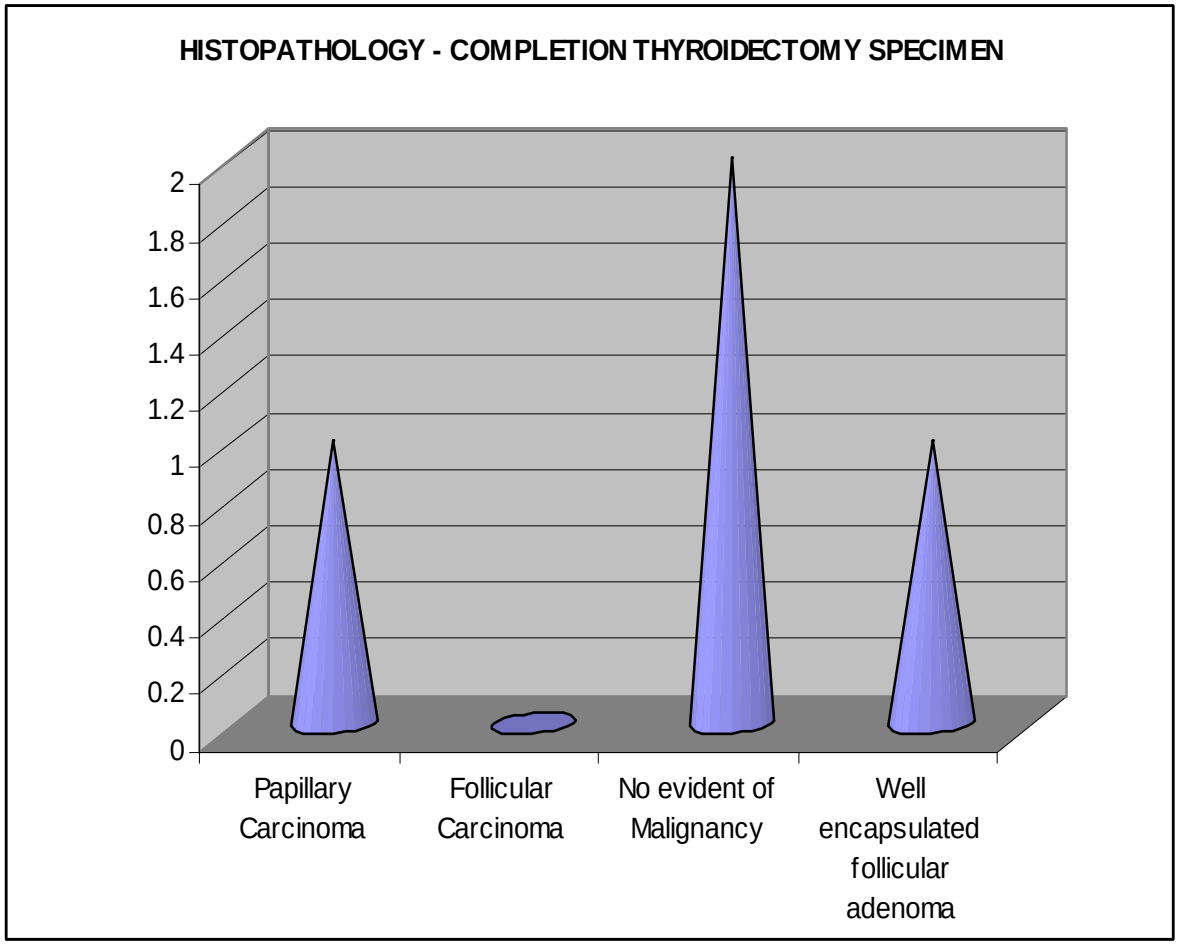
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1.8
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1.4
1.2
1
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0.6
0.4
0.2
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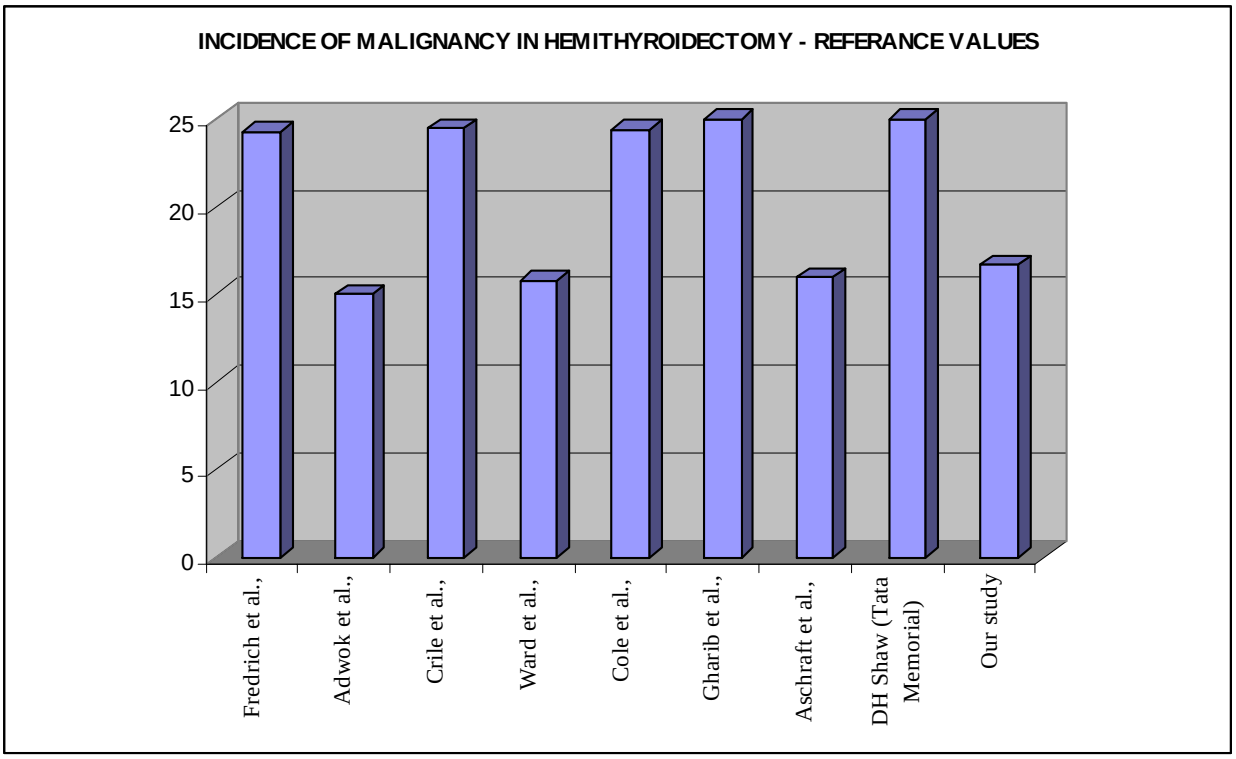
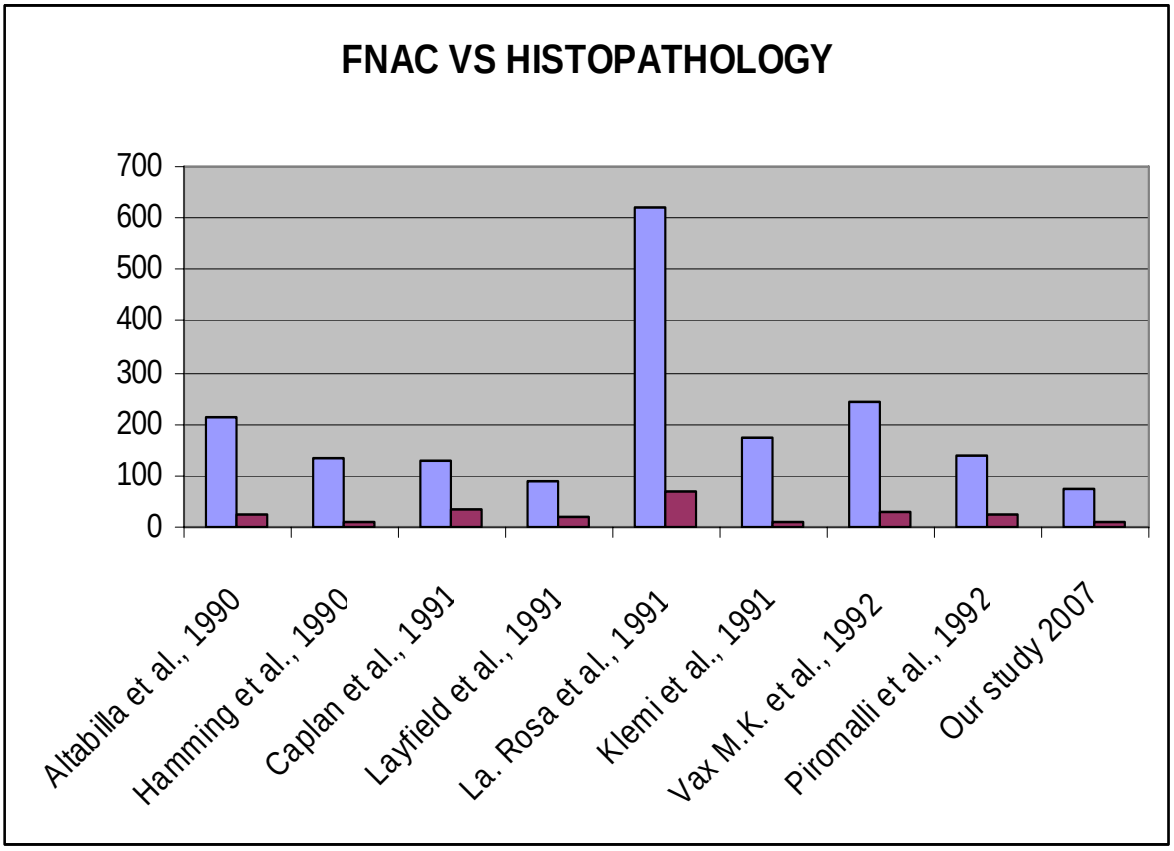
Papillary Carcinoma
Follicular Carcinoma
No evident of Malignancy
Well encapsulated follicular adenoma


INCIDENCE OF MALIGNANCY IN HEMITHYROIDECTOMY - REFERANCE VALUES
25
20
15
10
5
0
Fredrich et al.,
Adwok et al.,
Crile et al.,
Ward et al.,
Cole et al.,
Gharib et al.,
Aschraft et al.,
DH Shaw (Tata Memorial)
Our study


FNAC VS HISTOPATHOLOGY
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600
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300
200
100
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Altabilla et al., 1990
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La. Rosa et al., 1991
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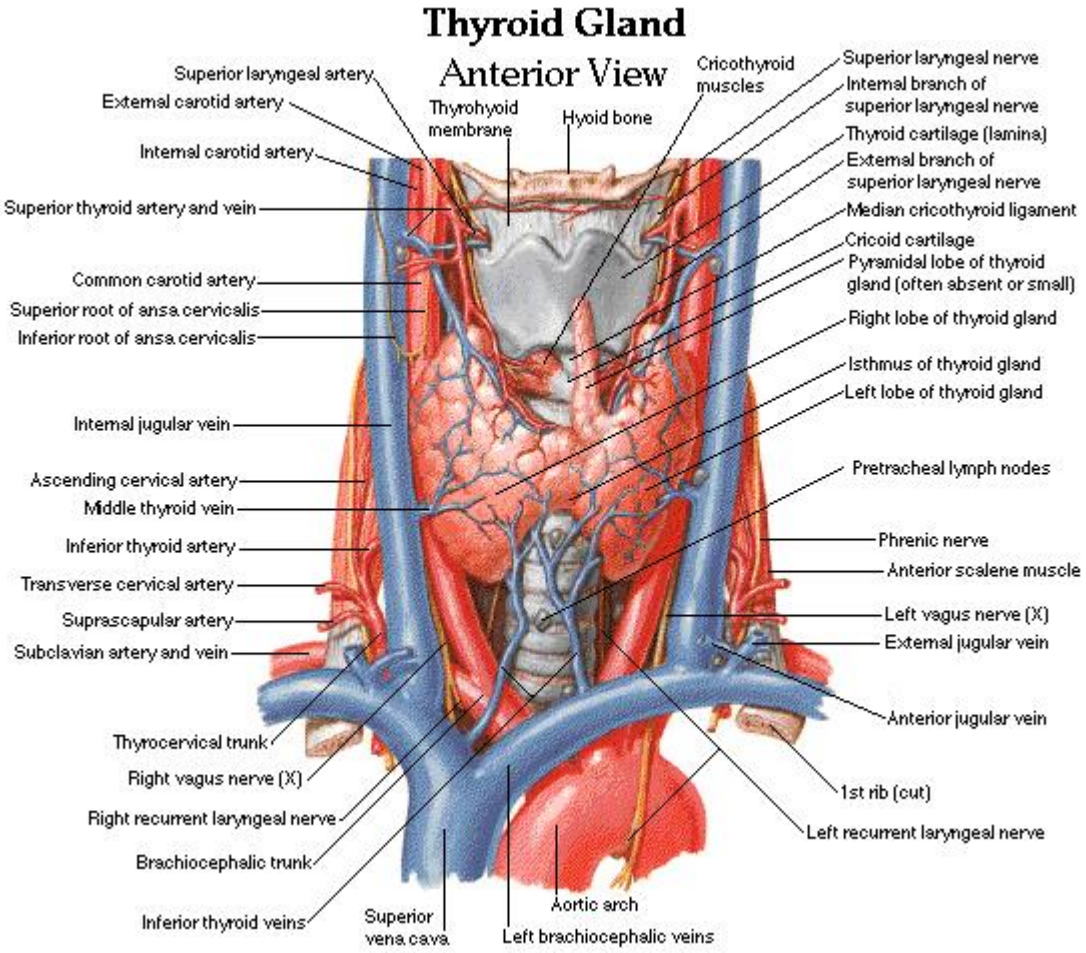
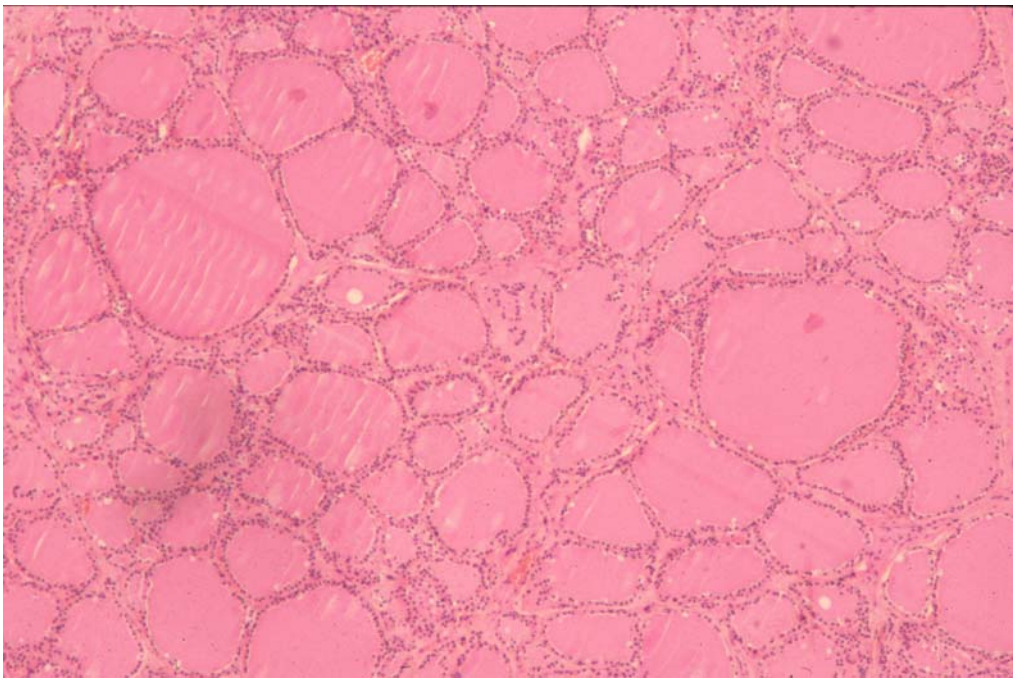
Vax M.K. et al., 1992
Piromalli et al., 1992
Our study 2007

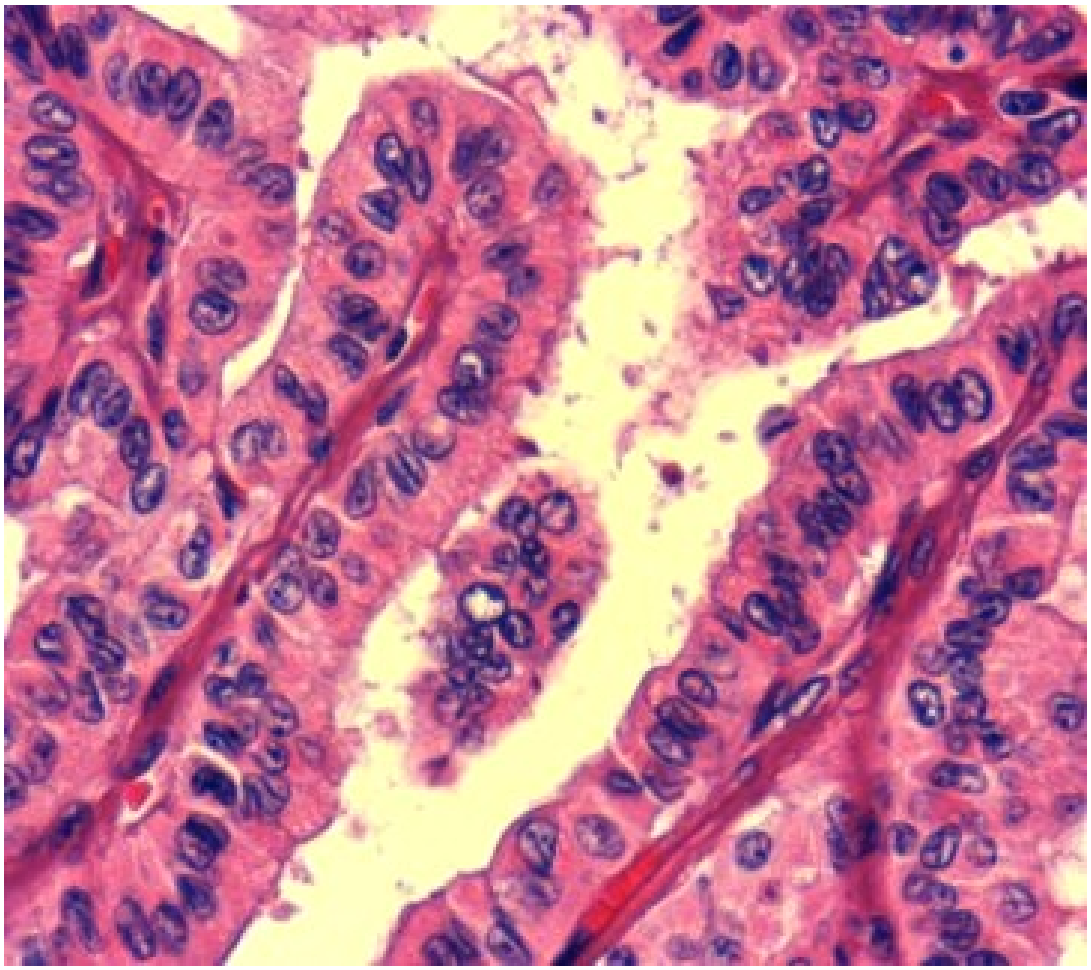
ANATOMY – RELATIONSHIP OF THYROID GLAND



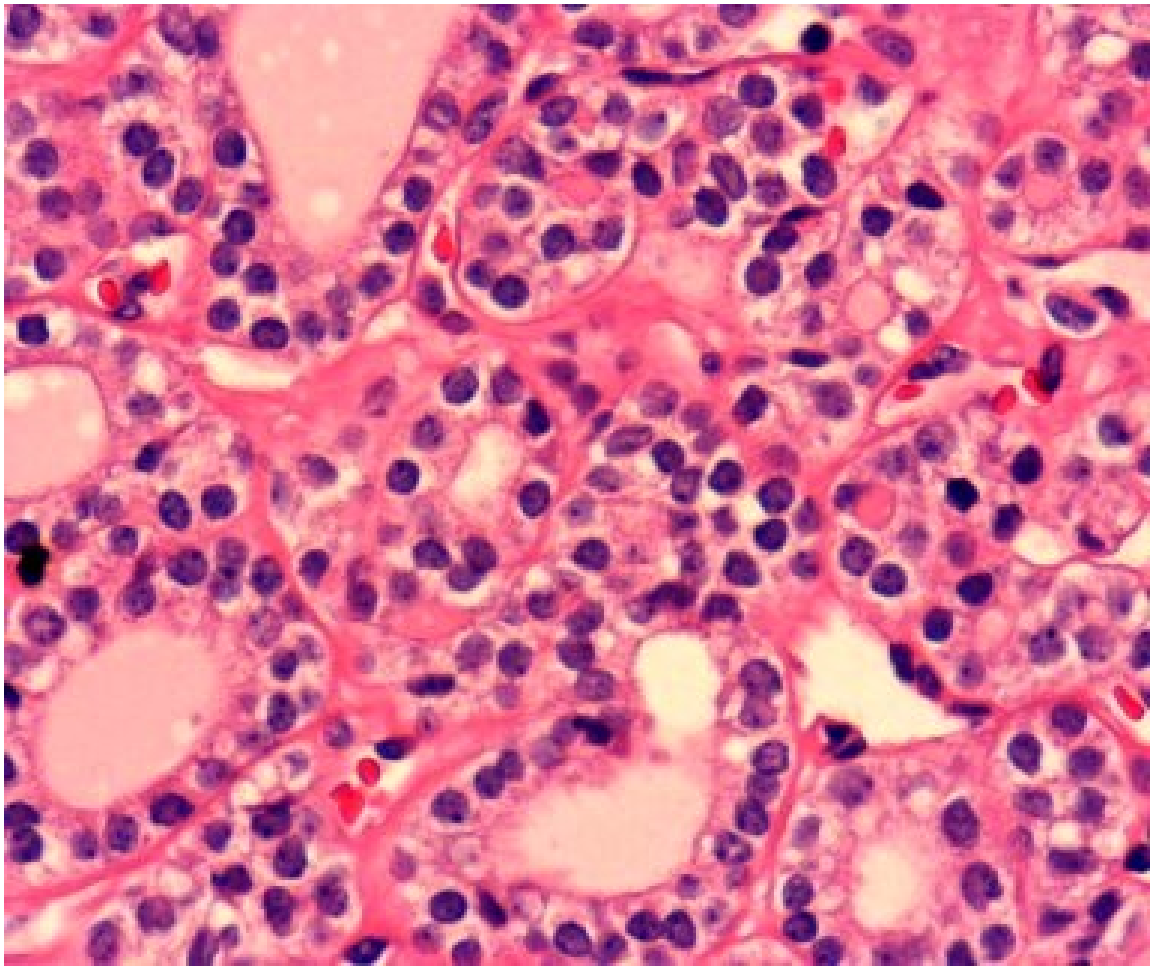
NORMAL THYROID FNAC



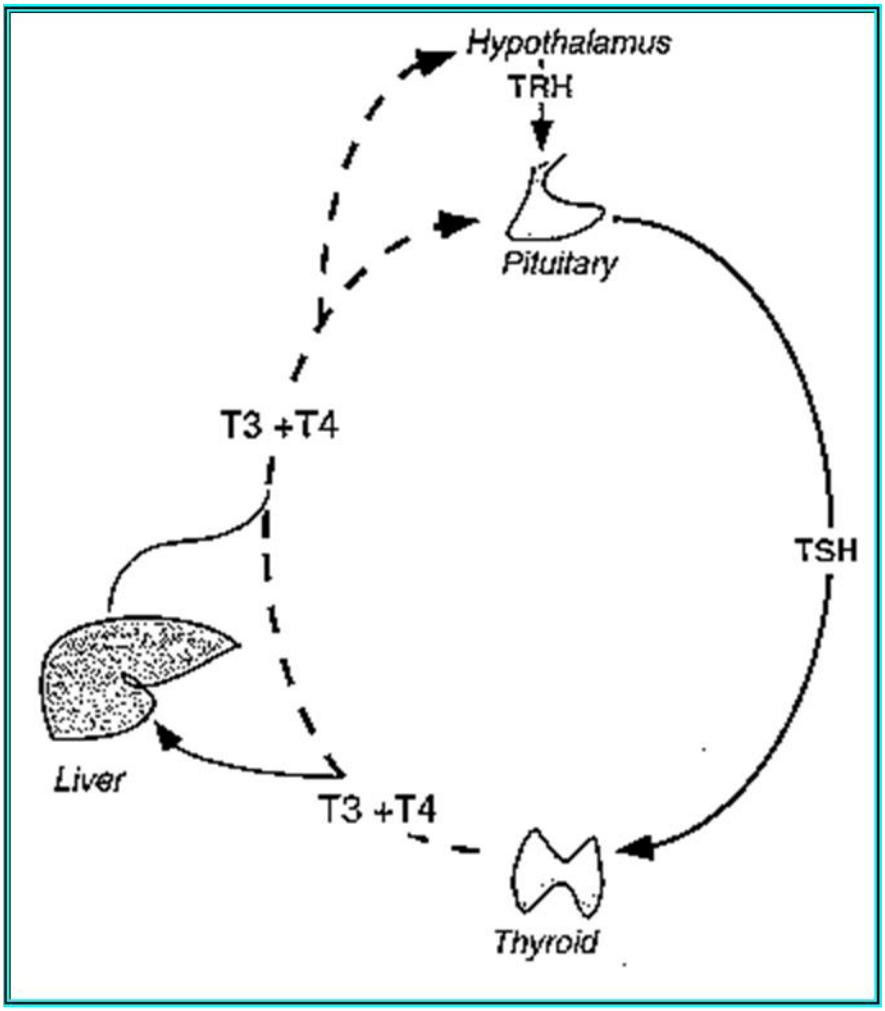
PAPILLARY CARCINOMA - THYROID



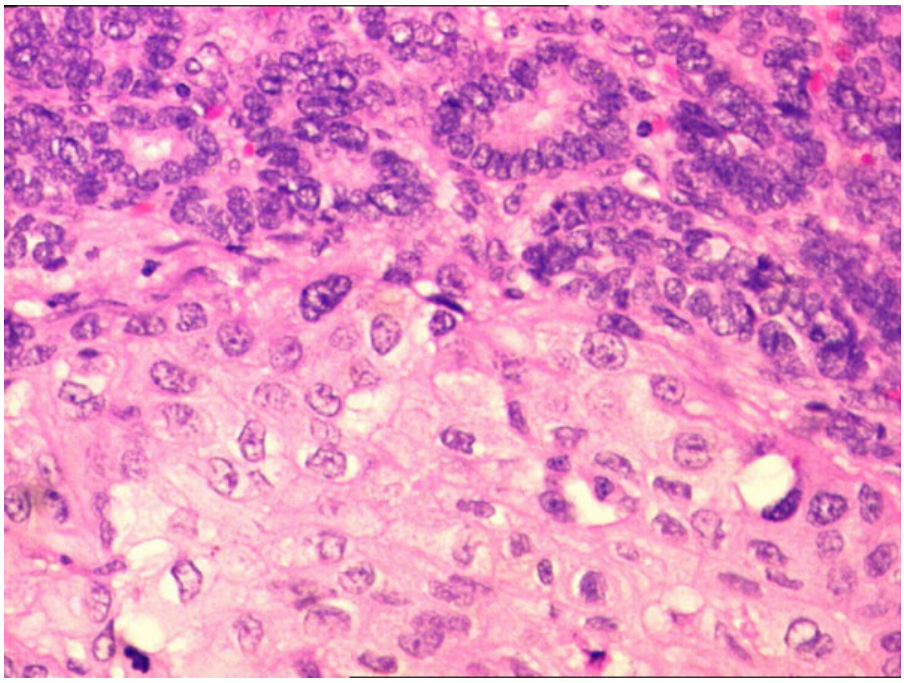
FOLLICULAR CARCINOMA - THYROID



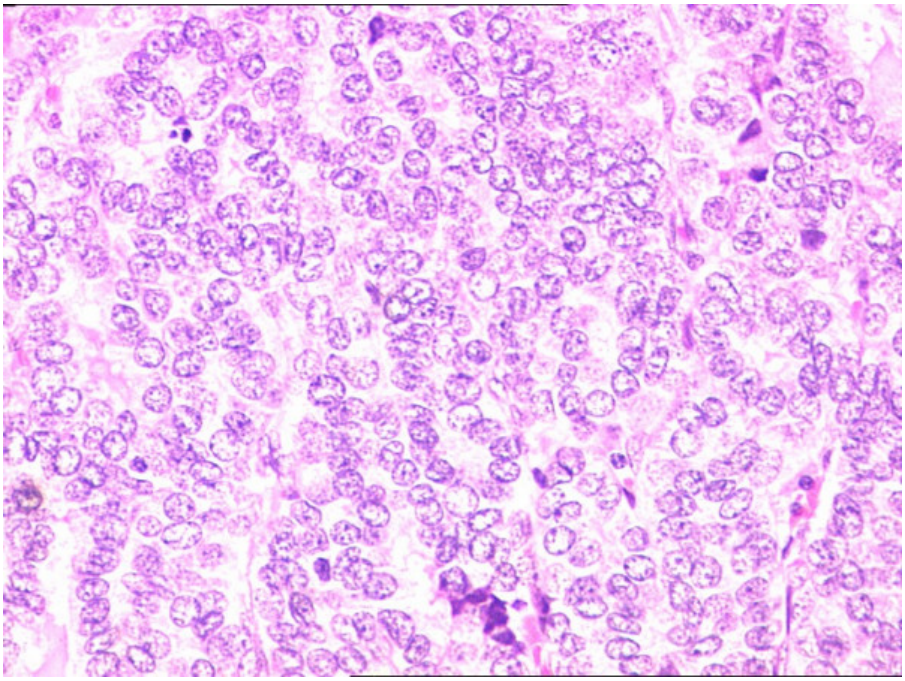
HYPOTHALAMO – PITUITARY – THYROID AXIS



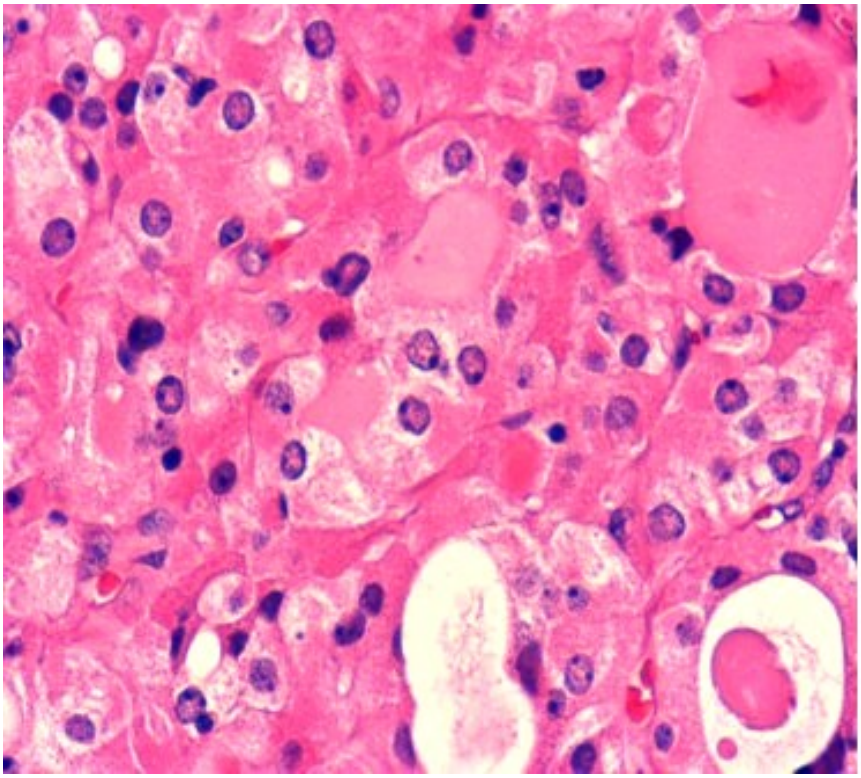
FOLLICULAR VARIANT OF PAPILLARY CARCINOMA



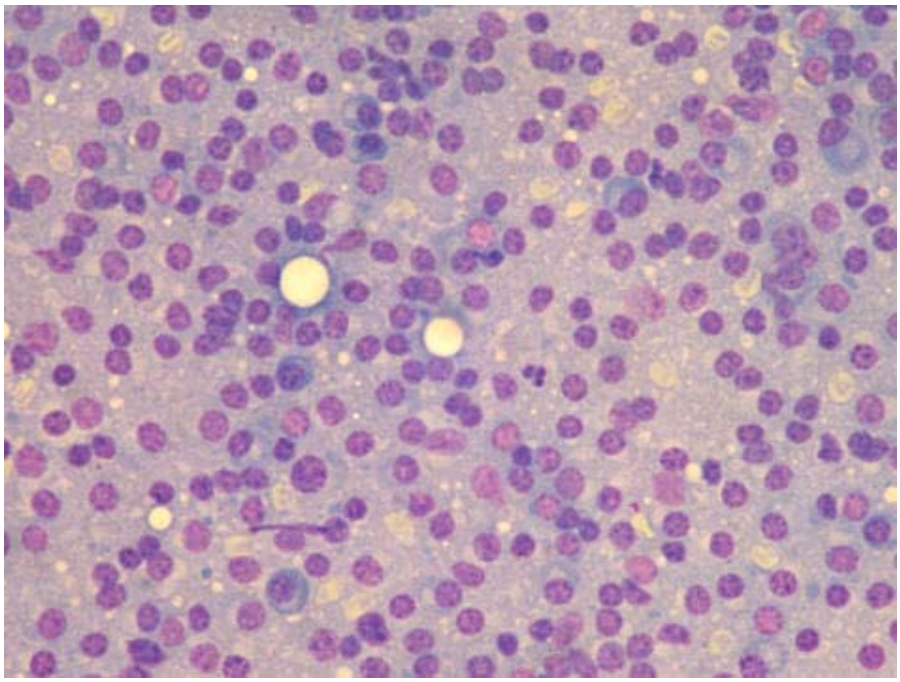
PAPILLARY CARCINOMA WITH NUCLEAR CROWDING AND NUCLEAR GROOVING



HURTHLE CELL CARCINOMA



THYROID LYMPHOMA



A CASE OF SOLITARY NODULE RIGHT LOBE OF THYROID